

Exhibit 4

April 17, 2006

More Sensitive, Quicker Test Developed for Cholera and Botulism

The current test for botulin—the potent neurotoxin responsible for paralyzing botulism—involves injecting a mouse with a suspicious sample and waiting to see if it dies. The test is crude, imprecise and can take up to three days to deliver results. But after 72 hours death may have already come for victims of the deadly toxin. Now researchers have discovered an exquisitely sensitive test that kills no animals and takes just three hours to complete.

Biophysicists Jeffrey Mason of the Armed Forces Institute of Pathology, Timothy O'Leary of the Veterans Health Administration and their colleagues paired specific antibodies for botulin and cholera with the crime scene DNA-amplification technique known as polymerase chain reaction, or PCR. By combining the two, the scientists can detect trace amounts of the biological agents in urine samples, water or other mediums. "We can actually detect down to 10 molecules of biotoxin in a sample," Mason notes. "We're always below 500 molecules."

But the test also improves on its predecessors by delivering fewer false positives. Previous attempts to couple antibodies and PCR often led to incorrect results due to DNA contamination from the lab or instruments involved. So the scientists encased the antibody and DNA in a liposome, a man-made fat cell capable of sheltering up to 60 copies of DNA fragments. Since the important DNA is protected, the entire sample can be subjected to rigorous cleaning to remove any DNA contamination, Mason notes.

The new test is quick and as much as 1,000 times more sensitive in detecting cholera or botulin than any other assay, according to the paper presenting the research in yesterday's *Nature Biotechnology*. "The goal is to develop something small



and portable—a lab on a chip version," Mason adds.

It also holds wider promise: if antibodies can be found for other biological agents, like the poison ricin, the same technique could be employed. And, by modifying the liposome, it could even potentially be useful in early detection of disease. "The goal is to use this to detect disease biomarkers in [the bloodstream], particularly cancer," Mason says. "We're able to check such low levels that this would be a very powerful technique, because most cancer markers are only present in very low concentrations."

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